

12-10-03



PHA 6157.2 (3085/1)  
PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of Ng et al.  
Serial No. 10/647,866  
Filed August 25, 2003  
For PROCESS FOR PREPARATION OF 9,11-EPOXY STEROIDS AND  
INTERMEDIATES USEFUL THEREIN

December 9, 2003

COMMISSIONER FOR PATENTS  
P.O. BOX 1450  
ALEXANDRIA, VIRGINIA 22313-1450

SIR:

INFORMATION DISCLOSURE STATEMENT

\* In accordance with 37 C.F.R. 1.97 and 1.98 and MPEP 609, and in compliance with the duty of disclosure set forth in 37 C.F.R. 1.56, applicants submit the attached PTO/SB/08A for consideration by the Patent and Trademark Office in the above-entitled application and to be made of record therein.

The references listed on the attached PTO/SB/08A have been previously submitted in parent application Serial No. 10/112,355 and, therefore, in accordance with MPEP 609, are not being provided at this time.

This Information Disclosure Statement is being submitted pursuant to 37 C.F.R. §1.97(b) in that applicants believe that it is being filed prior to the mailing date of the first Office action on the merits. Accordingly, neither a statement nor fee under 37 C.F.R. §1.97(c) or (d) is required. However, if an Office action was issued prior to the date of mailing of this Information Disclosure Statement, the Commissioner is hereby authorized to charge any required fees regarding this Information Disclosure Statement to Deposit Account No. 19-1345.

PHA 6157.2 (3085/1)  
PATENT

Respectfully submitted,

*Patricia K. Fitzsimmons*

Patricia K. Fitzsimmons, Reg. No. 52,894  
SENNIGER, POWERS, LEAVITT & ROEDEL  
One Metropolitan Square, 16th Floor  
St. Louis, Missouri 63102  
(314) 231-5400

PKF/kl1

Express Mail Label No. EV 272755531 US

PTO/SB/08A		<b>Complete if Known</b>	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)		Application Number	10/647,866
		Filing Date	August 25, 2003
		Confirmation Number	not yet assigned
		First Named Inventor	Ng et al.
		Group Art Unit	not yet assigned
		Examiner Name	not yet assigned
Sheet 1 of 4	Attorney Docket No.	PHA 6157.2 (3085/1)	

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. <sup>1</sup>	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY
		Number	Kind Code <sup>2</sup> (if known)		
	1	3,053,856	B1	Payne et al.	09-11-1962
	2	3,200,113	B1	Christiansen et al.	08-10-1965
	3	3,300,489	B1	Holden et al.	01-24-1967
	4	3,413,288	B1	Creger et al.	11-26-1968
	5	3,759,791	B1	Marsheck et al.	09-18-1973
	6	3,897,417	B1	Warnant et al.	07-29-1975
	7	3,972,878	B1	Schirmann et al.	08-03-1976
	8	4,118,488	B1	Philippon et al.	10-03-1978
	9	4,270,994	B1	Behling	06-02-1981
	10	4,559,332	B1	Grob et al.	12-17-1985
	11	5,565,588	B1	Batist et al.	10-15-1996
	12	5,616,742	B1	Fu et al.	04-01-1997

Examiner Signature		Date Considered	
--------------------	--	-----------------	--

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup>Unique citation designation number. <sup>2</sup>See attached Kinds of U.S. Patent Documents. <sup>3</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup>For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup>Applicant is to place a check mark here if English language Translation is attached or place an "A" here if English language abstract is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.

PTO/SB/08A			<b>Complete if Known</b>		
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)			Application Number	10/647,866	
			Filing Date	August 25, 2003	
			Confirmation Number	not yet assigned	
			First Named Inventor	Ng et al.	
			Group Art Unit	not yet assigned	
			Examiner Name	not yet assigned	
Sheet	2	of	4	Attorney Docket No.	PHA 6157.2 (3085/1)

### FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	T <sup>6</sup>
		Office	Number <sup>4</sup>	Kind Code <sup>2</sup> (if known)			
	13	DE	2404947		Roussel UCLAF	08-22-1974	
	14	DE	2349022	A1	Andor et al.	05-31-1977	
	15	DE	2443746	A1	Searle & Co.	10-11-1976	
	16	DE	2932925	A1	Gist Brocades NV	05-12-1981	
	17	EP	122 232	A1	Ciba Geigy Corp.	12-17-1985	
	18	EP	123 734	A1	Gist Brocades NV	11-07-1984	
	19	EP	165 902	A2	Ciba Geigy Corp	02-06-1987	
	20	WO	97/21720	A2	G.D. Searle and Co.	06-19-1997	

### OTHER ART - NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>6</sup>
	21	Abstract 084228, "Hydroxylated Androstane Production From Sterols", Chemical Abstracts, Vol. 100, No. 11, p. 430, March 12, 1984 and JP 58 179 498 A (Danippon Ink and Chemicals, Inc.); Japan, October 20, 1983	
	22	ARIAS et al., "Epoxidation of Alkenes With Trichloroacetonitrile/Hydrogen Peroxide In A Neutral Biphasic Solvent System", <i>J. Org. Chem.</i> , Vol. 48, pp. 888-890, 1983	

Examiner Signature		Date Considered	
--------------------	--	-----------------	--

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup>Unique citation designation number. <sup>2</sup>See attached Kinds of U.S. Patent Documents. <sup>3</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup>For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup>Applicant is to place a check mark here if English language Translation is attached or place an "A" here if English language abstract is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.

PTO/SB/08A		<b>Complete if Known</b>	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)		Application Number	10/647,866
		Filing Date	August 25, 2003
		Confirmation Number	not yet assigned
		First Named Inventor	Ng et al.
		Group Art Unit	not yet assigned
		Examiner Name	not yet assigned
Sheet 3 of 4	Attorney Docket No.	PHA 6157.2 (3085/1)	

23	BROWN et al., "Steroidal Aldosterone Blockers VII", <i>J. Med. Chem.</i> , Vol. 6, pp. 732-735, 1963
24	BROWN et al., "Steroidal Aldosterone Blockers III", <i>J. Org. Chem.</i> , Vol. 25, No. 1, pp. 96-99, 1960
25	CARRUTHERS et al., "Synthesis Of Corticoids From 9 $\alpha$ -Hydroxyandrost-4-ene-8,17-dione", <i>J. Org. Chem.</i> , Vol. 57, pp. 961-965, 1992
26	CHRISTIANSEN et al., "The Reaction Of Steroidal 4,6-dien-3-ones With Cyanide", <i>Steroids</i> , Vol. 1, No. 6, pp. 620-627, June 1963
27	Database WPI, Section Ch, Week 8145, Derwent Publications, Ltd., London, GB; Class B01, AN 81-82258D and JP 56 120 697 A (Mitsubishi Chem. Ind. Ltd.), September 22, 1981
28	DEGASPARO et al., "Antialdosterones: Incidence And Prevention Of Sexual Side Effects", <i>J. Steroid Biochem</i> , Vol. 32, No 13, pp. 223-227, 1989
29	DEGASPARO et al., "Three New Epoxy-Spirolactone Derivatives: Characterization <i>in Vivo</i> and <i>in Vitro</i> ", <i>The Journal Of Pharmacology And Experimental Therapeutics</i> , Vol. 240, No. 2, pp. 650-656, 1987
30	DESHAYES, "Utilisation De Modèles Mathématiques Pour l'optimisation En Fermentation. Applicatoin Aux Transfor-mations Par Les Micro-organismes", <i>Bulletine De La Societe Chimique De France 2 Partie - Chimie Organique, Biochimie</i> , No. 1-2, pp. 24-34, May 18, 1979 (translation)
31	GABRIEL, S., "Condensationsproducte aus Phtalsaeureanhydrid", <i>Ber.</i> , pp. 1389-1396, 1884
32	GROB et al., "Steroidal, Aldosterone Antagonists. Increased Selectivity of 9 $\alpha$ ,11-Epoxy Derivatives", <i>Helvetica Chimica Acta</i> , Vol. 80, No. 2, pp. 566-585, March 24, 1997
33	HELLBERG et al., "5 $\alpha$ -Hydroxy-3 $\alpha$ -Cholestanecarboxylic Lactone", <i>OPPI Briefs</i> , Volume 15, No. 3, pp. 154-156, 1983
34	NAGATA et al., "Angular-Substituted Polycyclic Compounds. I. Cyanation Of $\Delta$ -Cholesten-3-one", <i>Journal Of Organic Chemistry</i> , Volume 26, pp. 2413-2420, 1961.
35	NAGATA et al., "Hydrocyanation, VI. Application Of The New Hydrocyanation Methods To Conjugate Hydrocyanation Of $\alpha,\beta$ -Unsaturated Ketones, Conjugated Dienones, And Conjugated Enamines And To Preparation Of $\alpha$ -Cyanohydrins", <i>J. Amer. Chem. Soc.</i> , Vol. 94:13, pp. 4654-4672, 1972.

Examiner Signature	Date Considered
--------------------	-----------------

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup>Unique citation designation number. <sup>2</sup>See attached Kinds of U.S. Patent Documents. <sup>3</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup>For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup>Applicant is to place a check mark here if English language Translation is attached or place an "A" here if English language abstract is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.

PTO/SB/08A		<b>Complete if Known</b>	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)		Application Number	10/647,866
		Filing Date	August 25, 2003
		Confirmation Number	not yet assigned
		First Named Inventor	Ng et al.
		Group Art Unit	not yet assigned
		Examiner Name	not yet assigned
Sheet 4 of 4	Attorney Docket No.	PHA 6157.2 (3085/1)	

36	NICKISCH et al., "Aldosterone Antagonists.3.Synthesis and Activities of Steroidal 7 $\alpha$ -(Alkoxycarbonyl)-15,16-Methylene Methylene Spirolactones", <i>Journal of Medicinal Chemistry</i> , Vol. 33, No. 2, pp. 509-513, February 1990
37	OGATA et al., "The Alkali Phosphate-Catalyzed Epoxidation And Oxidation By A Mixture Of Nitrile And Hydrogen Peroxide", <i>Tetrahedron</i> , Vol. 20, pp. 2065-2068, 1964
38	OGATA, "The Kinetics Of The Phosphate/Catalyzed Epoxidation Of Styrenes With A Mixture Of Nitrile & Hydrogen Peroxide", <i>Bull. Chem. Soc. Of Japan</i> , Vol. 38, No. 2, pp. 194-199, 1965
39	PAYNE et al., "Reactions of Hydrogen Peroxide. VII. Alkali-Catalyzed Epoxidation and Oxidation Using A Nitrile As Co-reactant", <i>J. Org. Chem.</i> , Vol. 26, pp. 659-663, 1961
40	PETERSON et al., "Microbiological Transformations of Steroids. VI. Preparation of 11 $\alpha$ -Hydroxy-6-dehydroproges-terone", <i>Journal Of The American Chemical Society</i> , Vol. 75, No. 2, pp. 419-421, January 29, 1953
41	TURNER et al., "Applications Of High-potential Quinones. Part I. The Mechanism Of Dehydrogenation Of Steroidal Ketones By 2,3 Dichloro-5,6-dicyanobenzoquinone", <i>J. Chem. Soc.</i> , pp. 1720-1730, 1967.
42	VAN LEUSEN et al., "Chemistry of Sulfonylmethyl Isocyanides. 33. Synthesis of 17-(isocyanotosylmethylene) Steroids: Precursors To Pregnane Derivatives" <i>Recueil Des Travaux Chimiques Des Pays-Bas</i> , Vol. 110, No. 10, pp. 393-401, October 1991
43	WEIR et al., "7 $\alpha$ -Carboalkoxy Steroidal Spirolactones As Aldosterone Antagonists", <i>Journal of Medicinal Chemistry</i> , Vol. 18, No. 8, pp. 817-821, August 1975

Examiner Signature	Date Considered
--------------------	-----------------

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup>Unique citation designation number. <sup>2</sup>See attached Kinds of U.S. Patent Documents. <sup>3</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup>For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup>Applicant is to place a check mark here if English language Translation is attached or place an "A" here if English language abstract is attached..

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.